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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HADDAD, MAHER M	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 01/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/935,124	LORENS ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,14-16,19,28 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,14,15,19,28 and 29* is/are rejected.

7)☒ Claim(s) *16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 12/6/04, is acknowledged.

2. Claims 1, 6, 14-16, 19, and 28-29 are pending and under examination.

3. In view of the amendment filed on 12/6/04, only the following rejection is remained.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 6, 14-15, 19 and 28-29 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for identifying a compound that modulates angiogenesis comprising contacting the compound with a cell expressing the ILKAP polypeptide of SEQ ID NO: 2 and determining the angiogenic or loss of angiogenesis phenotypic effect of the compound upon the cell expressing the ILKAP polypeptide, whereby the difference in the angiogenic or loss of angiogenesis effect as compared to the angiogenic or loss of angiogenesis effect in the absence of the compound indicates that the compound modulates angiogenesis. does not reasonably provide **enablement** for a method for identifying a compound that modulates angiogenesis comprising contacting the compound with a cell expressing an ILKAP polypeptide , wherein the ILKAP polypeptide "has at least 90% identity to an amino acid sequence of SEQ ID NO:2", and wherein the ILKAP polypeptide has an anti-angiogenic phenotype in claim 1, wherein the ILDAMP polypeptide "has at least 95% identity to an amino acid sequence of SEQ ID NO: 2" in claim 28. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Action mailed 6/03/04.

Applicant's arguments, filed 12/6/04, have been fully considered, but have not been found persuasive.

Applicant submits that the level of identity (not "homology") required by the claims is intended to encompass other naturally occurring variants and alleles of human ILKAP that retain the anti-angiogenic activity of SEQ ID NO:2, as well as closely related orthologs that can be used in the assays of the invention. Further, the level of identity is intended to encompass variants engineered for ease of experimental manipulation—for example, variants that include amino acids that can be modified so that the polypeptide can be more easily purified. Applicant asserts that Applicants are not attempting to "predict" the function of related proteins, but to provide coverage for polypeptides with minor sequence variations.

The Examiner notes that the word "identity" is not defined in the specification. Further the Examiner notes that the term "encompass" in the asserted intended definition of the level of

identity, is open-ended, it would read on other sequence identities such as paralogous, xenologous, convergent evolution among others. Thus, the term "encompass" does not preclude sequence "homology". Finally, the orthologous identity is sequence identity due to descent from a common locus (i.e., a homology sequence relationship due to an implied common implied shared evolutionary history, i.e., "homology").

Applicant argues with respect to Atwood et al that the claims in the instant application do not refer to "some degree of similarity" bit require a strict identity (at least 90%) between the claimed polypeptides and the reference sequence. Further, Applicant submits that Skolnick et al the difference between the terms "homology", refereeing to evolutionarily related sequences, and "identity," which requires an exact match in amino acid sequence, not evolutionarily conserved substitutions. Applicant submits that the cited references are taken out of contact by the examiner, as they teach that functional activity cannot be easily assigned to a polypeptide based only on "similarity" or "homology." Applicant dismisses both Atwood and Skolnick references as "this situation does not apply to the present application." Applicant asserts that the claims are not attempting to predict a function based on sequence similarity or homology, rather the claims encompass specific minor variants of a reference sequence, where the variants can be tested to ensure that they retain the claimed functional activity. Applicant assets that the level of skilled artisan is high. Applicant submits that in view of Metzler et al the skilled practitioner can easily predict the effect of altering an amino acid on the function of the protein.

However, both sequence identity/similarity provide a quantitative explicit mapped relationship among sequences in a procedure of comparing two or more sequences. Further, similarity is an observable quantity that might be express as percent identity and the homology is refers to a conclusion drawn from these data that two genes share a common evolutionary history. Given Applicant's specification lacks a definition for "identity" and Applicant asserted intended meaning of "identity" does not preclude homology and similarity, then the cited references are relevant to the claimed invention. Applicant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. The claims as written encompass a broad genus of polypeptides with an unlimited number of possibilities with regard to the length of the polypeptide sequence. Further, the enablement issues of making the protein still remain because the specification does not teach and provide sufficient guidance as to which amino acid of SEQ ID NO:2 would have been altered such that the resultant polypeptide would have retained the function of anti-angiogenic phenotype. In addition, variation up to 10% of SEQ ID NO: 2 would be (39^{20}), which provide a range of activities, not all which are necessarily predictive of promoting adhesion. Furthermore, increasing the number of substitutions additively increases the probability that the protein will be inactivated. Therefore, absent the ability to predict which of these polypeptides would function as claimed, and given the lack of data on regions critical for activity, for one of skill in the art to practice the invention as claimed would require a level of experimentation that is excessive and undue.

Applicant directs the examiner's attention to Example 1 to deliver the point that the skilled practitioner would likely avoid making significant changes to the PP2C-like phosphatase domain, which conferred anti-angiogenic activity to a partial ILKAP clone. However, the

specification fails to point to a specific domain for the activity of the ILKAP in the anti-angiogenesis phenotype. Example 1 refers to ILKAP expressing cells and to PP2C family. Therefore, given the lack of data on regions critical for activity, for one of skill in the art to practice the invention as claimed would require a level of experimentation that is excessive and undue.

Applicant refers to MPEP 2164.08 and the Training Materials for Examining Patent Applications with respect to 112, first paragraph-Enablement. Applicant submits that one of skill in the art has only to identify polypeptides using well-known sequence algorithms, that have at least 90% identity to a conserved reference sequence. Applicant submits that although many such [nucleic] amino acids are possible, one of skill can readily determine one by one, any particular ILKAP polypetide, without undue experimentation.

Again, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Therefore, one skilled in the art at the time of the invention would not be able to predict which positions in the protein which are tolerant to change that will not result in abolishing the anti-angiogenic activity of the polypeptide. Consequently the skilled artisan would not know how to use the instant invention as broadly claimed. While experimental testing techniques using appropriate constructs and transform cells are available, it is not routine in the art to use such methods when the expectation of success is unpredictable based on the instant disclosure. Thus, it would require an undue amount of experimentation of one skilled in the art to practice the invention as broadly claimed.

6. Claim 16 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maher Haddad, Ph.D.
Patent Examiner
January 19, 2005

Christina Chan

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